

SEQUENCE LISTING

<110> JCR Pharmaceuticals Co., Ltd.

<120> Mutant human alpha-N-acetyl glucosaminidase and use thereof

<130> 1233JP

<150> P2020-145100

<151> 2020-08-28

<160> 67

<170> PatentIn version 3.5

<210> 1

<211> 720

<212> PRT

<213> Homo sapiens

<400> 1

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
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Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp

500

505

510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
 515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
 530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
 545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
 565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
 580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val Ser
 595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
 610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
 625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
 645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
 660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
 675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
 690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 2
<211> 2229
<212> DNA
<213> Homo sapiens

<400> 2
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ggaagctgg	2229

<210> 3
 <211> 720
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 1

<400> 3

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
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Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Glu Ser Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val

385		390		395		400
Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val						
		405		410		415
Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr						
		420		425		430
Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu						
		435		440		445
Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His						
		450		455		460
Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn						
465		470		475		480
Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg						
		485		490		495
Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp						
		500		505		510
Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala						
		515		520		525
Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala						
		530		535		540
Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr						
545		550		555		560
Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala						
		565		570		575
Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg						
		580		585		590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 4
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 1, synthetic
sequence

<400> 4
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ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc	240
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gtggccttga ggcgcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac	480
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gctttagggt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct	600
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 ggaagctgg 2229

<210> 5
 <211> 721
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 2

<400> 5

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 1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
 20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
 35 40 45

Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala
 50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
195 200 205

Asp Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu

260

265

270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
 275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
 290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
 305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
 325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
 340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
 355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
 370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
 385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
 405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
 420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
 435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
 450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val
595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
705 710 715 720

Trp

<210> 6
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 2, synthetic
sequence

<400> 6
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cggagcgcct atttatccaa agagctggcc tctttactga gggctggagg cgtgctggct	1800
tatgagctgc tccccgcttt agatgagggt ttagctagcg actctcgttt ttactggga	1860
tcttggctgg agcaagctcg tgccgctgcc gtgagcgaag ccgaggccga tttctatgag	1920
cagaactccc ggtaccagct gacactctgg ggccccgagg gcaacattct ggactacgcc	1980
aacaagcagc tggctggact ggtggccaac tactacaccc ctcgttggag gctgttttta	2040

gaagctcttg tcgactccgt ggccaaggt atccccctcc aacagcacca gttcgacaag 2100
aatgtgttcc agctggaaca agctttcgtg ctgtccaaac aaaggtaccc ctcccagccc 2160
cggggagaca cagtggatct ggccaagaag atcttttttaa agtattaccc tcggtgggtg 2220
gctggaagct gg 2232

<210> 7
<211> 720
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of hNAGLU mutant type 16

<400> 7

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu

115

120

125

Gln Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
 130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
 145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
 165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
 180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
 195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
 210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
 225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
 245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
 260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
 275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
 290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
 305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys	Lys	Ile	Phe	Leu	Lys	Tyr	Tyr	Pro	Arg	Trp	Val	Ala	Gly	Ser	Trp
705					710					715					720

<210> 8
 <211> 2229
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> nucleic acid sequence coding hNAGLU mutant type 16, synthetic sequence

<400> 8
 atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
 gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
 ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
 ggttttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240
 actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac 300
 gtggcttgga gcggcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa 360
 ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat 420
 tccttcgtgt ggtgggactg ggctcgttgg gaacaggaga tcgactggat ggccctcaac 480
 ggaattaatc tggcttttagc ttgggtccggc caagaggcca tttggcagag ggtgtacctc 540
 gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct 600
 tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt 660
 aagcaactgt atttacagca tcgtgtgctc gatcagatga ggtccttcgg catgacaccc 720
 gtgctccccg cttttgctgg ccacgtcccc gaagctgtca ctctgtgtgt tcctcaagtt 780
 aacgtgacaa agatgggctc ttggggccac tttaactgca gctacagctg ttccttttta 840
 ctggcccccg aggatcccat ttttcccatc atcggtccc tctttttaag ggagctgatc 900
 aaagagttcg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct 960
 agcagcgagc ctagctatct agctgctgcc accacagccg tctatgaggc catgaccgcc 1020
 gtggacaccg aagctgtgtg gctgctgcaa ggttggctgt tccagcacca gcctcagttc 1080

tggggcccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctcggggtcg tctgctggtc	1140
ctcgatctgt tcgctgagtc ccaacccgtt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaacttt ggcggaaacc acggactgtt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg cccccaagg catttcccag aatgagggtg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cggtcccgat ttagctgctt gggtgacctc cttcgctgct	1440
cggaggatatg gcgtgtccca tcccgatgcc ggagctgctt ggaggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560
ccttctttac agatgaatac cagcatctgg tacaaccgga gcgacgtgtt cgaagcttgg	1620
cggtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta	1680
ttagatctga ctcgtcaagc tgtgcaagaa ctgggtgtctt tatactacga ggaagctcgg	1740
agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat	1800
gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct	1860
tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag	1920
aactcccggg accagctgac actctggggc cccgagggca acattctgga ctacccaac	1980
aagcagctgg ctggactggg ggccaactac tacacccctc gttggaggct gtttttagaa	2040
gctctggtcg actccgtggc ccaaggatat cccttccaac agcaccagtt cgacaagaat	2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtacccctc ccagccccgg	2160
ggagacacag tggatctggc caagaagatc tttttaaagt attacctcg gtgggtggct	2220
ggaagctgg	2229

<210> 9

<211> 720

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 3

<400> 9

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 10

<211> 2229

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 3, synthetic
sequence

<400> 10

atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60

gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120

ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc	180
ggttttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc	240
actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac	300
gtggcttgga gcggcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac	480
ggaattaatc tggcttttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc	540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgt	600
tggggacgga tgggcaatth acacacttgg gatggccctc tcccccttc ttggcacatt	660
aagcaactgt atttacagca tcgtgtgctc gatcggatga ggtccttcgg catgacaccc	720
gtgctccccg cttttgctgg ccacgtcccc gaagctgtca ctcgtgtgtt tcctcaagtt	780
aacgtgacaa agatgggctc ttggggccac ttttaactgca gctacagctg ttccttttta	840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgac	900
aaagagttag gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
agcagcgagc ctagctatth agctgctgcc accacagccg tctatgaggc catgaccgcc	1020
gtggacaccg aagctgtgtg gctgctgcaa ggttggctgt tccagcacca gcctcagttc	1080
tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctcggggtcg tctgctggtc	1140
ctcgatctgt tcgctgagtc ccaaccggtt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaactth ggcggaacc acggactgtt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg ccccggaagg catttcccag aatgagggtg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cggtcccgat ttagctgctt gggtagacct cttcgtgct	1440
cggaggatatg gcgtgtccca tcccgatgcc ggagctgctt ggaggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560

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ccttcttttac agatgaatac cagcatctgg tacaaccgga gcgacgtggt cgaagcttgg      1620
cgtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta      1680
ttagatctga ctcgtcaagc tgtgcaagaa ctggtgtctt tatactacga ggaagctcgg      1740
agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat      1800
gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct      1860
tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag      1920
aactcccggg accagctgac actctggggc cccgagggca acattctgga ctacgccaac      1980
aagcagctgg ctggactggg ggccaactac tacaccctc gttggaggct gtttttagaa      2040
gctctggtcg actccgtggc ccaaggatc cccttccaac agcaccagtt cgacaagaat      2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg      2160
ggagacacag tggatctggc caagaagatc tttttaaagt attaccctc gtgggtggct      2220
ggaagctgg                                     2229

```

```

<210> 11
<211> 720
<212> PRT
<213> Artificial Sequence

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```

<220>
<223> amino acid sequence of hNAGLU mutant type 4

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```

<400> 11

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Asp Glu Ala Arg Glu Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1           5           10          15

```

```

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20           25           30

```

```

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35           40           45

```

```

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50           55           60

```

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Lys Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu

645

650

655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
 660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
 675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
 690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
 705 710 715 720

<210> 12

<211> 2229

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 4, synthetic
 sequence

<400> 12

atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
 gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
 ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
 ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240
 actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac 300
 gtggcttgga gcggcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa 360
 ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat 420
 tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac 480
 ggaattaatc tggctttagc ttgggtccggc caagaggcca tttggcagag ggtgtacctc 540
 gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct 600

tggggacgga tgggcaatth acacacttgg gatggccctc tcccccttc ttggcacatt	660
aagcaactgt atttacagca tcgtgtgctc gatcagatga ggtccttcgg catgacaccc	720
gtgctccccg cttttgctgg ccacgtcccc aaagctgtca ctcgtgtgtt tcctcaagtt	780
aacgtgacaa agatgggctc ttggggccac ttttaactgca gctacagctg ttccttttta	840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgac	900
aaagagtctg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
agcagcgagc ctagctatth agctgctgcc accacagccg tctatgaggc catgaccgcc	1020
gtggacaccg aagctgtgtg gctgctgcaa ggttggctgt tccagacca gcctcagttc	1080
tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctcggggctg tctgctggtc	1140
ctcgatctgt tcgtgagtc ccaaccgctt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaactth ggcggaacc acggactgtt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg ccccggaagg catttcccag aatgaggctg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cgttcccgat ttagctgctt gggtagacct cttcgctgct	1440
cggaggatat gcgtgtccca tcccgatgcc ggagctgctt ggagggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560
ccttctttac agatgaatac cagcatctgg tacaaccgga gcgacgtgtt cgaagcttgg	1620
cgtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta	1680
ttagatctga ctcgtcaagc tgtgcaagaa ctgggtgtct tatactacga ggaagctcgg	1740
agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat	1800
gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct	1860
tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag	1920
aactcccggg accagctgac actctggggc cccgagggca acattctgga ctacccaac	1980
aagcagctgg ctggactggg ggccaactac tacacccctc gttggaggct gtttttagaa	2040
gctctggctg actccgtggc ccaaggatat cccttccaac agcaccagtt cgacaagaat	2100

gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg 2160
ggagacacag tggatctggc caagaagatc tttttaaaagt attaccctcg gtgggtggct 2220
ggaagctgg 2229

<210> 13
<211> 720
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of hNAGLU mutant type 17

<400> 13

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Val
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala

515

520

525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
 530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
 545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
 565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
 580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val Ser
 595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
 610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
 625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
 645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
 660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
 675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
 690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
 705 710 715 720

<210> 14
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 17, synthetic sequence

<400> 14
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gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
ggccccggtc ccgtgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
ggttttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240
actggtgtgg ccgtgctgc tggactccat cgttatttac gggatttctg tggatgccac 300
gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa 360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat 420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac 480
ggaattaatc tggcttttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc 540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgt 600
tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt 660
aagcaactgt atttacagca tcgtgtgctc gatcagatga ggtccttcgg catgacaccc 720
gtgctccccg cttttgctgg ccacgtcccc gaagctgtca ctggtgtgtt tcctcaagtt 780
aacgtggtca agatgggctc ttggggccac tttaactgca gctacagctg ttccttttta 840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgata 900
aaagagtctg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct 960
agcagcgagc ctagctatct agctgctgcc accacagccg tctatgaggc catgaccgcc 1020
gtggacaccg aagctgtgtg gctgtgcaa ggttggctgt tccagcacca gcctcagttc 1080
tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctgggggtcg tctgctggtc 1140

ctcgatctgt tcgctgagtc ccaacccgtt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaacttt ggcggaacc acggactggt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg cccccaagg catttcccag aatgaggtgg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cggtcccgat ttagctgctt gggtgacctt cttcgtgct	1440
cggaggatatg gcgtgtccca tcccgatgcc ggagctgctt ggaggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560
ccttctttac agatgaatac cagcatctgg tacaaccgga gcgacgtgtt cgaagcttgg	1620
cgtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta	1680
ttagatctga ctcgtcaagc tgtgcaagaa ctggtgtctt tatactacga ggaagctcgg	1740
agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat	1800
gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct	1860
tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag	1920
aactcccggg accagctgac actctggggc cccgagggca acattctgga ctacgccaac	1980
aagcagctgg ctggactggg ggccaactac tacaccctc gttggaggct gtttttagaa	2040
gctctggtcg actccgtggc ccaaggtatc cccttccaac agcaccagtt cgacaagaat	2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg	2160
ggagacacag tggatctggc caagaagatc tttttaaggt attaccctcg gtgggtggct	2220
ggaagctgg	2229

<210> 15
 <211> 720
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 5

<400> 15

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Pro
305 310 315 320

Asp Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val

385		390		395		400
Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val						
		405		410		415
Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr						
		420		425		430
Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu						
		435		440		445
Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His						
		450		455		460
Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn						
		465		470		480
Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg						
		485		490		495
Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp						
		500		505		510
Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala						
		515		520		525
Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala						
		530		535		540
Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr						
		545		550		560
Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala						
		565		570		575
Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg						
		580		585		590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 16
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 5, synthetic
sequence

<400> 16
atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
ggccccgggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180

ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc	240
actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac	300
gtggccttga ggcgcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac	480
ggaattaatc tggcttttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc	540
gctttagggt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct	600
tggggacgga tgggcaatth acacacttgg gatggccctc tcccccttc ttggcacatt	660
aagcaactgt atttacagca tcgtgtgctc gatcagatga ggtccttcgg catgacaccc	720
gtgctccccg cttttgctgg ccacgtcccc gaagctgtca ctcgtgtgtt tcctcaagtt	780
aacgtgacaa agatgggctc ttggggccac ttttaactgca gctacagctg ttccttttta	840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgac	900
aaagagtctg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
agcagcgagc ctagctatth agctgctgcc accacagccg tctatgaggc catgaccgcc	1020
gtggacccccg acgctgtgtg gctgctgcaa ggttggctgt tccagcacca gcctcagttc	1080
tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctcggggctg tctgctggtc	1140
ctcgatctgt tcgctgagtc ccaaccggtt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaactth ggcggaacc acggactgtt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg ccccggaagg catttcccag aatgagggtg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cgthcccgat ttagctgctt gggtgacctc cttcgctgct	1440
cggaggtatg gcgtgtccca tcccgatgcc ggagctgctt ggagggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560
ccttctttac agatgaatac cagcatctgg tacaaccgga gcgacgtgtt cgaagcttgg	1620

cgtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta 1680
 ttagatctga ctcgtcaagc tgtgcaagaa ctggtgtctt tatactacga ggaagctcgg 1740
 agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat 1800
 gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct 1860
 tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag 1920
 aactccccgt accagctgac actctggggc cccgagggca acattctgga ctacgccaac 1980
 aagcagctgg ctggactggt ggccaactac tacaccctc gttggaggct gtttttagaa 2040
 gctctggtcg actccgtggc ccaaggatat cctttccaac agcaccagtt cgacaagaat 2100
 gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg 2160
 ggagacacag tggatctggc caagaagatc tttttaaagt attaccctcg gtgggtggct 2220
 ggaagctgg 2229

<210> 17
 <211> 720
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 6

<400> 17

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
 1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
 20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
 35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
 50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe

260

265

270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
 275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
 290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
 305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
 325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
 340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
 355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
 370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
 385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
 405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
 420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
 435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
 450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
 465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
 485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ala Val Trp Tyr Asn Arg Ser Asp
 500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
 515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
 530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
 545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
 565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
 580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
 595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
 610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
 625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
 645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 18
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 6, synthetic
sequence

<400> 18
atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240
actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac 300
gtggcttgga gcggcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa 360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat 420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac 480
ggaattaatc tggctttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc 540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct 600
tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt 660

aagcaactgt atttacagca tcgtgtgctc gatcagatga ggtccttcgg catgacaccc	720
gtgctccccg cttttgctgg ccacgtcccc gaagctgtca ctcgtgtgtt tcctcaagtt	780
aacgtgacaa agatgggctc ttggggccac ttttaactgca gctacagctg ttccttttta	840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgac	900
aaagagtctg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
agcagcgagc ctagctatatt agctgctgcc accacagccg tctatgaggc catgaccgcc	1020
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aagcagctgg ctggactggg ggccaactac tacacccctc gttggaggct gtttttagaa	2040
gctctggctg actccgtggc ccaaggtatc cccttccaac agcaccagtt cgacaagaat	2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtacccctc ccagccccgg	2160

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ggaagctgg 2229

<210> 19

<211> 720

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 7

<400> 19

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala

130

135

140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
 145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
 165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
 180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
 195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
 210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
 225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
 245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
 260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
 275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
 290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
 305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
 325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Asn Leu Thr
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 20
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 7, synthetic sequence

<400> 20
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gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240
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gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa 360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat 420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac 480
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gctttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgt 600
tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt 660
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tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctgggggtcg tctgctggtc 1140
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cccttcatct ggtgcatgct gcacaacttt ggcggaaacc acggactggt cggagcttta	1260
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aagcagctgg ctggactggg ggccaactac tacaccctc gttggaggct gtttttagaa	2040
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gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg	2160
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ggaagctgg	2229

<210> 21

<211> 720

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 18

<400> 21

Asp Glu Ala Arg Glu Ala Ala Val Arg Ala Leu Val Ala Arg Leu

1	5	10	15
Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala	20	25	30
Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly	35	40	45
Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala	50	55	60
Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp	65	70	75
Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly	85	90	95
Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val	100	105	110
Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu	115	120	125
Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala	130	135	140
Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly	145	150	155
Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu	165	170	175
Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro	180	185	190
Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp	195	200	205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Gln Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 22
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 18, synthetic
sequence

<400> 22
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ggccccgggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc 240

actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac	300
gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
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ggaattaatc tggctttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc	540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct	600
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ccttctttac agatgaatac cagcatctgg tacaaccgga gcgacgtgtt cgaagcttgg	1620
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aactccccgt accagctgac actctggggc cccgagggca acattctgga ctacgccaac      1980
aagcagctgg ctggactggg ggccaactac tacacccctc gttggaggct gtttttagaa      2040
gctctggtcg actccgtggc ccaaggatat cccttccaac agcaccagtt cgacaagaat      2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg      2160
ggagacacag tggatctggc caagaagatc tttttaaaagt attaccctcg gtgggtggct      2220
ggaagctgg                                     2229

```

```

<210> 23
<211> 720
<212> PRT
<213> Artificial Sequence

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```

<220>
<223> amino acid sequence of hNAGLU mutant type 19

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<400> 23

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```

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1           5           10          15

```

```

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20          25          30

```

```

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35          40          45

```

```

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50          55          60

```

```

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65          70          75          80

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Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln Lys Arg Val Leu Asp
195 200 205

Gln Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His

660

665

670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
 675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
 690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
 705 710 715 720

<210> 24

<211> 2229

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 19, synthetic sequence

<400> 24

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ggccccggtc ccgtgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc      180
ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc      240
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gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa      360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat      420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac      480
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gctttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgt      600
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ggaagctgg

2229

<210> 25
<211> 720
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of hNAGLU mutant type 8

<400> 25

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
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Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Glu Ser Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
 145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
 165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
 180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
 195 200 205

Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
 210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
 225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
 245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
 260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
 275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
 290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
 305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
 325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala

530

535

540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
 545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
 565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
 580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
 595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
 610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
 625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
 645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
 660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
 675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
 690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
 705 710 715 720

<210> 26

<211> 2229

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 8, synthetic sequence

<400> 26

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ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctgagtcc      180
ggtttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc      240
actggtgtgg ccgctgtctg tggactccat cgttatttac gggatttctg tggatgccac      300
gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa      360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat      420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac      480
ggaattaatc tggctttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc      540
gctttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct      600
tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt      660
aagcaactgt atttacagca tcgtgtgctc gatcggatga ggtccttcgg catgacaccc      720
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tggggccccg ctcaaattcg tgccgtgctg ggccgctgc ctcggggtcg tctgctggtc     1140
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cccttcatct ggtgcatgct gcacaacttt ggcggaacc acggactgtt cggagcttta     1260
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aactcccggg accagctgac actctggggc cccgagggca acattctgga ctacgccaac	1980
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gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtacccctc ccagccccgg	2160
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ggaagctgg	2229

<210> 27
 <211> 721
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 9

<400> 27

Asp	Glu	Ala	Arg	Glu	Ala	Ala	Ala	Val	Arg	Ala	Leu	Val	Ala	Arg	Leu
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Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
35 40 45

Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala
50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met

405

410

415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
 420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
 435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
 450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
 465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
 485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
 500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
 515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
 530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
 545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
 565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
 580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
 595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
705 710 715 720

Trp

<210> 28
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 9, synthetic
sequence

<400> 28
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cacgtggctt ggagcggcag ccaactgagg ctccctaggc ctctgcccgc tgtccccggt	360
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aacggaatta atctggcttt agcttgggtcc ggccaagagg ccatttggca gaggggtgtac	540
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cggagcgcct atttatccaa agagctggcc tctttactga gggctggagg cgtgctggct	1800
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gctggaagct gg	2232

<210> 29
 <211> 720
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> amino acid sequence of hNAGLU mutant type 10

<400> 29

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Leu	Gly	Pro	Gly	Pro	Ala	Ala	Asp	Phe	Ser	Val	Ser	Val	Glu	Arg	Ala
		20					25						30		

Leu	Ala	Ala	Lys	Pro	Gly	Leu	Asp	Thr	Tyr	Ser	Leu	Gly	Gly	Gly	Gly
	35					40					45				

Ala	Ala	Arg	Val	Arg	Val	Arg	Gly	Ser	Thr	Gly	Val	Ala	Ala	Ala	Ala
	50				55					60					

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe

260

265

270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
 275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
 290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Pro
 305 310 315 320

Asp Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
 325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
 340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
 355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
 370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
 385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
 405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
 420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
 435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
 450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 30

<211> 2229

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 10, synthetic
sequence

<400> 30

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ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc	180
ggttttagaca cctactccct cggcggagga ggagctgcta gggttcgtgt tcgtggatcc	240
actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac	300
gtggcttgga gcggcagcca actgaggctc ctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac	480
ggaattaatc tggctttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc	540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgct	600
tggggacgga tgggcaattt acacacttgg gatggccctc tcccccttc ttggcacatt	660

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aaagagtctg gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
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cccttcatct ggtgcatgct gcacaacttt ggcggaacc acggactgtt cggagcttta	1260
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gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct	1860
tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag	1920
aactcccgt accagctgac actctggggc cccgagggca acattctgga ctacccaac	1980
aagcagctgg ctggactggg ggccaactac tacacccctc gttggaggct gtttttagaa	2040
gctctggctg actccgtggc ccaaggtatc cccttccaac agcaccagtt cgacaagaat	2100
gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtacccctc ccagccccgg	2160

ggagacacag tggatctggc caagaagatc tttttaagt attacctcg gtgggtggct 2220

ggaagctgg 2229

<210> 31

<211> 721

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 11

<400> 31

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Glu Ser Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
35 40 45

Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala
50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu

130

135

140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
 145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
 165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
 180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
 195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
 210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
 225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
 245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
 260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
 275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
 290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
 305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
 325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
705 710 715 720

Trp

<210> 32
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 11, synthetic
sequence

<400> 32
atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
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ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctgagtcc 180
ggtttagaca cctactccct ctctggcgga ggaggagctg ctagggttcg tgttcgtgga 240
tccactgggtg tggccgctgc tgctggactc catcgttatt tacgggattt ctgtggatgc 300
cacgtggctt ggagcggcag ccaactgagg ctccctaggc ctctgcccgc tgtccccggt 360
gaactgaccg aggctacccc caatcggtac cgggtactacc agaacgtgtg cacccaaagc 420
tattccttcg tgtggtggga ctgggctcgt tgggaaaggg agatcgactg gatggccctc 480
aacggaatta atctggcttt agcttggtcc ggccaagagg ccatttggca gagggtgtac 540
ctcgccttag gttaaacaca agctgagatc aacgaattct tcaccggccc cgcttttctc 600
gcttggggac ggatgggcaa ttacacact tgggatggcc ctctcccccc ttcttggcac 660
attaagcaac tgtatttaca gcatcgtgtg ctcgatcgga tgaggtcctt cggcatgaca 720
cccgtgctcc ccgcttttgc tggccacgtc cccgaagctg tcactcgtgt gtttcctcaa 780
gttaacgtga caaagatggg ctcttggggc cactttaact gcagctacag ctgttccttt 840
ttactggccc ccgaggatcc catttttccc atcatcggct ccctcttttt aaggagctg 900
atcaaagagt tcggcaccga ccacatttac ggcgccgaca cttttaacga gatgcagccc 960
cctagcagcg agcctagcta tttagctgct gccaccacag ccgtctatga ggccatgacc 1020
gccgtggaca ccgaagctgt gtggctgctg caaggttggc tgttccagca ccagcctcag 1080

ttctggggcc ccgctcaaat tcgtgccgtg ctgggcgccg tgcctcgggg tcgtctgctg	1140
gtcctcgatc tgttcgctga gtcccaaccc gtttacacaa ggacagcctc cttccaaggt	1200
cagcccttca tctggtgcat gctgcacaac tttggcgga accacggact gttcggagct	1260
ttagaggctg tgaatggcgg acccgaagct gcccggctgt tccccaactc caccatgggtg	1320
ggaaccggaa tggccccga aggcatttcc cagaatgagg tggcttacag cctcatggcc	1380
gagctcggat ggcggaagga tcccgttccc gatttagctg cttgggtgac ctccttcgct	1440
gctcggagggt atggcgtgtc ccatcccgat gccggagctg cttggagggtt attattacgt	1500
tccgtctaca actgctccgg cgaggcttgc cggggacata atcgggtcccc tttagtctgt	1560
aggccttctt tacagatgaa taccagcatc tgggtacaacc ggagcgacgt gttcgaagct	1620
tggcgtttat tactgacatc cgctccctct ttagctacca gccccgcctt tcgttatgat	1680
ttattagatc tgactcgtca agctgtgcaa gaactgggtgt ctttatacta cgaggaagct	1740
cggagcgcct atttatccaa agagctggcc tctttactga gggctggagg cgtgctggct	1800
tatgagctgc tccccgcttt agatgagggtt ttagctagcg actctcgttt tttactggga	1860
tcttggctgg agcaagctcg tgccgctgcc gtgagcgaag ccgaggccga tttctatgag	1920
cagaactccc ggtaccagct gacactctgg ggccccgagg gcaacattct ggactacgcc	1980
aacaagcagc tggctggact ggtggccaac tactacaccc ctcgttggag gctgttttta	2040
gaagctctgg tcgactccgt ggcccaaggt atccccctcc aacagcacca gttcgacaag	2100
aatgtgttcc agctggaaca agctttcgtg ctgtccaaac aaaggtagcc ctcccagccc	2160
cggggagaca cagtggatct ggccaagaag atctttttaa agtattaccc tcggtgggtg	2220
gctggaagct gg	2232

<210> 33

<211> 720

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 12

<400> 33

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Gly Gly Gly Gly
35 40 45

Ala Ala Arg Val Arg Ile Arg Gly Ser Thr Gly Val Ala Ala Ala Ala
50 55 60

Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala Trp
65 70 75 80

Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro Gly
85 90 95

Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn Val
100 105 110

Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp Glu
115 120 125

Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu Ala
130 135 140

Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu Gly
145 150 155 160

Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe Leu
165 170 175

Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu Pro
180 185 190

Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu Asp
195 200 205

Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala Gly
210 215 220

His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val Thr
225 230 235 240

Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser Phe
245 250 255

Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu Phe
260 265 270

Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly Ala
275 280 285

Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr Leu
290 295 300

Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp Thr
305 310 315 320

Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro Gln
325 330 335

Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro Arg
340 345 350

Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val Tyr
355 360 365

Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met Leu
370 375 380

His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala Val
385 390 395 400

Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met Val
405 410 415

Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val Tyr
420 425 430

Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp Leu
435 440 445

Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser His
450 455 460

Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr Asn
465 470 475 480

Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val Arg
485 490 495

Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser Asp
500 505 510

Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu Ala
515 520 525

Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln Ala
530 535 540

Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala Tyr
545 550 555 560

Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu Ala
565 570 575

Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser Arg
580 585 590

Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Val Ser
595 600 605

Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Lys Tyr Gln Leu Thr
610 615 620

Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln Leu
625 630 635 640

Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe Leu
645 650 655

Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln His
660 665 670

Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu Ser
675 680 685

Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu Ala
690 695 700

Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser Trp
705 710 715 720

<210> 34
<211> 2229
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleic acid sequence coding hNAGLU mutant type 12, synthetic
sequence

<400> 34
atggaggctg tggccgtcgc cgccgctgtg ggcgtgctgc tgctggctgg cgctggcggc 60
gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120

ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc	180
ggttttagaca cctactccct cggcggagga ggagctgcta gggttcgtat tcgtggatcc	240
actggtgtgg ccgctgctgc tggactccat cgttatttac gggatttctg tggatgccac	300
gtggcttgga gcggcagcca actgaggctc cctaggcctc tgcccgtgt ccccggtgaa	360
ctgaccgagg ctacccccaa tcggtaccgg tactaccaga acgtgtgcac ccaaagctat	420
tccttcgtgt ggtgggactg ggctcgttgg gaaagggaga tcgactggat ggccctcaac	480
ggaattaatc tggcttttagc ttggtccggc caagaggcca tttggcagag ggtgtacctc	540
gcttttaggtt taacacaagc tgagatcaac gaattcttca ccggccccgc ttttctcgt	600
tggggacgga tgggcaatth acacacttgg gatggccctc tcccccttc ttggcacatt	660
aagcaactgt atttacagca tcgtgtgctc gatcggatga ggtccttcgg catgacaccc	720
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aacgtgacaa agatgggctc ttggggccac ttttaactgca gctacagctg ttccttttta	840
ctggcccccg aggatcccat ttttcccatc atcggctccc tctttttaag ggagctgac	900
aaagagttag gcaccgacca catttacggc gccgacacct ttaacgagat gcagccccct	960
agcagcgagc ctagctatth agctgctgcc accacagccg tctatgaggc catgaccgcc	1020
gtggacaccg aagctgtgtg gctgctgcaa ggttggctgt tccagacca gcctcagttc	1080
tggggccccg ctcaaattcg tgccgtgctg ggcgccgtgc ctcggggtcg tctgctggtc	1140
ctcgatctgt tcgctgagtc ccaaccggtt tacacaagga cagcctcctt ccaaggtcag	1200
cccttcatct ggtgcatgct gcacaactth ggcggaacc acggactgtt cggagcttta	1260
gaggctgtga atggcggacc cgaagctgcc cggctgttcc ccaactccac catggtggga	1320
accggaatgg ccccggaagg catttcccag aatgagggtg tctacagcct catggccgag	1380
ctcggatggc ggaaggatcc cggtcccgat ttagctgctt gggtagacct cttcgtgct	1440
cggaggatat gcgtgtccca tcccgatgcc ggagctgctt ggaggttatt attacgttcc	1500
gtctacaact gctccggcga ggcttgccgg ggacataatc ggtccccctt agttcgtagg	1560

ccttcttttac agatgaatac cagcatctgg tacaaccgga gcgacgtggt cgaagcttgg 1620
 cgtttattac tgacatccgc tccctcttta gctaccagcc ccgcctttcg ttatgattta 1680
 ttagatctga ctctgtcaagc tgtgcaagaa ctggtgtctt tatactacga ggaagctcgg 1740
 agcgcctatt tatccaaaga gctggcctct ttactgaggg ctggaggcgt gctggcttat 1800
 gagctgctcc ccgctttaga tgaggtttta gctagcgact ctcgtttttt actgggatct 1860
 tggctggagc aagctcgtgc cgctgccgtg agcgaagccg aggccgattt ctatgagcag 1920
 aactccaagt accagctgac actctggggc cccgagggca acattctgga ctacgccaac 1980
 aagcagctgg ctggactggg ggccaactac tacaccctc gttggaggct gtttttagaa 2040
 gctctggtcg actccgtggc ccaaggatc cccttccaac agcaccagtt cgacaagaat 2100
 gtgttccagc tggaacaagc tttcgtgctg tccaaacaaa ggtaccctc ccagccccgg 2160
 ggagacacag tggatctggc caagaagatc tttttaaagt attaccctc gtgggtggct 2220
 ggaagctgg 2229

<210> 35

<211> 721

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of hNAGLU mutant type 13

<400> 35

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
 1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
 20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
 35 40 45

Gly Ala Ala Arg Val Arg Ile Arg Gly Ser Thr Gly Val Ala Ala Ala
 50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe

645

650

655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
 660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
 675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
 690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
 705 710 715 720

Trp

<210> 36

<211> 2232

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 13, synthetic
 sequence

<400> 36

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 ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
 ggttttagaca cctactccct ctctggcgga ggaggagctg ctagggttcg tttcgtgga 240
 tccactgggtg tggccgctgc tgctggactc catcgttatt tacgggattt ctgtggatgc 300
 cacgtggctt ggagcggcag ccaactgagg ctccctaggc ctctgcccgc tgtccccggt 360
 gaactgaccg aggctacccc caatcggtac cgggtactacc agaactgtg caccctaaagc 420
 tattccttcg tgtggtggga ctgggctcgt tgggaaaggg agatcgactg gatggccctc 480

aacggaatta atctggcttt agcttgggtcc ggccaagagg ccatttggca gaggggtgtac	540
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gcttggggac ggatgggcaa tttaacacact tgggatggcc ctctcccccc ttcttggcac	660
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cagaactccc ggtaccagct gacactctgg ggccccgagg gcaacattct ggactacgcc	1980

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aatgtgttcc agctggaaca agctttcgtg ctgtccaaac aaaggtaccc ctcccagccc 2160
cggggagaca cagtggatct ggccaagaag atctttttaa agtattaccc tcggtgggtg 2220
gctggaagct gg 2232

<210> 37
<211> 721
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of hNAGLU mutant type 14

<400> 37

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
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Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
35 40 45

Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala
50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser

500

505

510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
 515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
 530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
 545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
 565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
 580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
 595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Lys Tyr Gln Leu
 610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
 625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
 645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
 660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
 675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
 690 695 700

Ala	Lys	Lys	Ile	Phe	Leu	Lys	Tyr	Tyr	Pro	Arg	Trp	Val	Ala	Gly	Ser
705					710					715					720

Trp

<210> 38
 <211> 2232
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> nucleic acid sequence coding hNAGLU mutant type 14, synthetic sequence

<400> 38
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 gccgccggcg acgaggctag ggaagccgcc gccgtgcggg ccctcgtggc taggctgctg 120
 ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc 180
 ggtttagaca cctactccct ctctggcgga ggaggagctg ctagggttcg tgttcgtgga 240
 tccactgggtg tggccgctgc tgctggactc catcgttatt tacgggattt ctgtggatgc 300
 cacgtggctt ggagcggcag ccaactgagg ctccctaggc ctctgcccgc tgtccccggt 360
 gaactgaccg aggctacccc caatcgggtac cgggtactacc agaacgtgtg cacccaaagc 420
 tattccttcg tgtggtggga ctgggctcgt tgggaaaggg agatcgactg gatggccctc 480
 aacggaatta atctggcttt agcttgggtc ggccaagagg ccatttggca gaggggtgtac 540
 ctcgcttttag gttaacaca agctgagatc aacgaattct tcaccggccc cgcttttctc 600
 gcttggggac ggatgggcaa ttacacact tgggatggcc ctctcccccc ttcttggcac 660
 attaagcaac tgtatttaca gcatcgtgtg ctcgatcgga tgaggtcctt cggcatgaca 720
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 gttaacgtga caaagatggg ctcttggggc cactttaact gcagctacag ctgttccttt 840
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atcaaagagt tcggcaccga ccacatttac ggcgccgaca cttttaacga gatgcagccc	960
cctagcagcg agcctagcta tttagctgct gccaccacag ccgtctatga ggccatgacc	1020
gccgtggaca ccgaagctgt gtggctgctg caaggttggc tgttccagca ccagcctcag	1080
ttctggggcc ccgtcaaat tcgtgccgtg ctgggcgccg tgcctcgggg tcgtctgctg	1140
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cagcccttca tctggtgcat gctgcacaac tttggcggaa accacggact gttcggagct	1260
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tcttggctgg agcaagctcg tgccgctgcc gtgagcgaag ccgaggccga tttctatgag	1920
cagaactcca agtaccagct gacactctgg ggccccgagg gcaacattct ggactacgcc	1980
aacaagcagc tggctggact ggtggccaac tactacaccc ctcgttggag gctgttttta	2040
gaagctctgg tcgactccgt ggcccaaggt atccccctcc aacagcacca gttcgacaag	2100
aatgtgttcc agctggaaca agctttcgtg ctgtccaaac aaaggtagcc ctcccagccc	2160
cggggagaca cagtggatct ggccaagaag atctttttaa agtattaccc tcggtgggtg	2220
gctggaagct gg	2232

<211> 721
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of hNAGLU mutant type 15

<400> 39

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala
20 25 30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
35 40 45

Gly Ala Ala Arg Val Arg Ile Arg Gly Ser Thr Gly Val Ala Ala Ala
50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val

355

360

365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
 370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
 385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
 405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
 420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
 435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
 450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
 465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
 485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
 500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
 515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
 530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
 545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Lys Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
705 710 715 720

Trp

<210> 40
<211> 2232
<212> DNA

<213> Artificial Sequence

<220>

<223> nucleic acid sequence coding hNAGLU mutant type 15, synthetic sequence

<400> 40

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ggccccggtc ccgctgccga tttttccgtg agcgtcgaga gggccctcgc tgctaagccc	180
ggtttagaca cctactccct ctctggcgga ggaggagctg ctagggttcg tattcgtgga	240
tccactgggtg tggccgctgc tgctggactc catcgttatt tacgggattt ctgtggatgc	300
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gaactgaccg aggctacccc caatcggtag cgggtactacc agaactgtgtg cacccaaagc	420
tattccttcg tgtggtggga ctgggctcgt tgggaaaggg agatcgactg gatggccctc	480
aacggaatta atctggcttt agcttggctc ggccaagagg ccatttggca gaggggtgtac	540
ctcgcttttag gtttaacaca agctgagatc aacgaattct tcaccggccc cgcttttctc	600
gcttggggac ggatgggcaa ttacacact tgggatggcc ctctcccccc ttcttggcac	660
attaagcaac tgtatttaca gcatcgtgtg ctcgatcgga tgaggtcctt cggcatgaca	720
cccgtgctcc ccgcttttgc tggccacgtc cccgaagctg tctctcgtgt gtttcctcaa	780
gttaacgtga caaagatggg ctcttggggc cactttaact gcagctacag ctgttccttt	840
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atcaaagagt tcggcaccga ccacatttac ggcgccgaca cttttaacga gatgcagccc	960
cctagcagcg agcctagcta tttagctgct gccaccacag ccgtctatga ggccatgacc	1020
gccgtggaca ccgaagctgt gtggctgctg caaggttggc tgttccagca ccagcctcag	1080
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cagaactcca agtaccagct gacactctgg ggccccgagg gcaacattct ggactacgcc	1980
aacaagcagc tggctggact ggtggccaac tactacaccc ctcgttggag gctgttttta	2040
gaagctctgg tcgactccgt ggcccaaggt atcccccttc aacagcacca gttcgacaag	2100
aatgtgttcc agctggaaca agctttcgtg ctgtccaaac aaaggtagcc ctcccagccc	2160
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gctggaagct gg	2232

<210> 41
 <211> 2285
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> nucleic acid sequence containing a gene coding hNAGLU, synthetic sequence

<400> 41	
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tggctggcgc tggcggcgcc gccggcgacg aggctaggga agccgccgcc gtgcgggccc	120

tcgtggctag gctgctgggc cccgggtcccg ctgccgattt ttccgtgagc gtcgagaggg	180
ccctcgctgc taagcccggg ttagacacct actccctcgg cggaggagga gctgctaggg	240
ttcgtgttcg tggatccact ggtgtggccg ctgctgctgg actccatcgt tatttacggg	300
atttctgtgg atgccacgtg gcttggagcg gcagccaact gaggctccct aggcctctgc	360
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tgtgcaccca aagctattcc ttcgtgtggg gggactgggc tcgttgggaa agggagatcg	480
actggatggc cctcaacgga attaactctgg ctttagcttg gtccggccaa gaggccattt	540
ggcagagggt gtacctcgt ttaggtttaa cacaagctga gatcaacgaa ttcttcaccg	600
gccccgcttt tctcgttgg ggacggatgg gcaatttaca cacttgggat ggccctctcc	660
ccccttcttg gcacattaag caactgtatt tacagcatcg tgtgctcgat cagatgaggt	720
ccttcggcat gacaccgctg ctccccgctt ttgctggcca cgtccccgaa gctgtcactc	780
gtgtgtttcc tcaagttaac gtgacaaaga tgggctcttg gggccacttt aactgcagct	840
acagctgttc ctttttactg gccccgagg atccccattt tcccatcatc ggctccctct	900
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agcaccagcc tcagttctgg gggccgctc aaattcgtgc cgtgctgggc gccgtgcctc	1140
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cctccttcca aggtcagccc ttcatctggt gcatgctgca caactttggc ggaaaccacg	1260
gactgttcgg agcttttagag gctgtgaatg gcggaccca agctgcccgg ctgttcccca	1320
actccaccat ggtgggaacc ggaatggccc ccgaaggcat ttcccagaat gaggtggtct	1380
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ggttattatt acgttccgtc tacaactgct ccggcgaggc ttgccgggga cataatcggt	1560
cccctttagt tcgtaggcct tctttacaga tgaataccag catctggtac aaccggagcg	1620

acgtgttcga agcttggcgt ttattactga catccgctcc ctcttttagct accagccccg	1680
ccttttcgtta tgatttatta gatctgactc gtcaagctgt gcaagaactg gtgtctttat	1740
actacgagga agctcggagc gcctatttat ccaaagagct ggccctcttta ctgagggtctg	1800
gaggcgtgct ggcttatgag ctgctccccg ctttagatga ggtttttagct agcgactctc	1860
gttttttact gggatcttgg ctggagcaag ctcgtgccgc tgccgtgagc gaagccgagg	1920
ccgattttcta tgagcagaac tcccgggtacc agctgacact ctggggcccc gagggcaaca	1980
ttctggacta cgccaacaag cagctggctg gactgggtggc caactactac acccctcgtt	2040
ggaggctgtt tttagaagct ctggctgact ccgtggccca aggtatcccc ttccaacagc	2100
accagttcga caagaatgtg ttccagctgg aacaagcttt cgtgctgtcc aaacaaaggt	2160
acccctccca gccccgggga gacacagtgg atctggccaa gaagatcttt ttaaagtatt	2220
accctcgggtg ggtggctgga agctggcatc accatcacca tcactaagcg gccgcaaaga	2280
cagaa	2285

<210> 42
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> MluI addition 5' primer

<400> 42	
ttttacgcgt cgccaccatg gagg	24

<210> 43
 <211> 58
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> His Tag-NotI addition 5' primer

<400> 43	
ttctgtcttt gcggccgctt agtgatgggtg atggatgatgc cagcttccag ccacccac	58

<210> 44
 <211> 27
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing K59E/P60S mutation, synthetic sequence

 <400> 44
 gtgtctaaac cggactcagc agcgagg 27

 <210> 45
 <211> 23
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing L67_G68insS mutation, synthetic
 sequence

 <400> 45
 ctcctccgcc agagagggag tag 23

 <210> 46
 <211> 25
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing R152Q mutation, synthetic sequence

 <400> 46
 cagtcgatct cctgttcca acgag 25

 <210> 47
 <211> 26
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing Q232R mutation, synthetic sequence

 <400> 47
 gaaggacctc atccgatcga gcacac 26

<210> 48
 <211> 22
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing E251K mutation, synthetic sequence

 <400> 48
 gagtgcacagc tttggggacg tg 22

 <210> 49
 <211> 26
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing T263V mutation, synthetic sequence

 <400> 49
 gagcccatct tgaccacgtt aacttg 26

 <210> 50
 <211> 25
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing T343P/E344D mutation, synthetic
 sequence

 <400> 50
 gccacacagc gtcgggggtcc acggc 25

 <210> 51
 <211> 29
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 5' primer for introducing S528A/I529V mutation, synthetic
 sequence

 <400> 51
 cagatgaata ccgccgtctg gtacaaccg 29

<210> 52
 <211> 29
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 5' primer for introducing S549N/A551T mutation, synthetic sequence

 <400> 52
 catccgctcc caatttaact accagcccc 29

 <210> 53
 <211> 24
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 5' primer for introducing D636Q mutation, synthetic sequence

 <400> 53
 gccgaggccc agttctatga gcag 24

 <210> 54
 <211> 25
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing H227K mutation, synthetic sequence

 <400> 54
 cgagcacacg cttctgtaaa tacag 25

 <210> 55
 <211> 23
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> 3' primer for introducing V77I mutation, synthetic sequence

 <400> 55
 ggatccacga atacgaaccc tag 23

<210> 56
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> 5' primer for introducing R643K mutation, synthetic sequence

<400> 56
gcagaactcc aagtaccagc tg 22

<210> 57
<211> 760
<212> PRT
<213> Homo sapiens

<400> 57

Met Met Asp Gln Ala Arg Ser Ala Phe Ser Asn Leu Phe Gly Gly Glu
1 5 10 15

Pro Leu Ser Tyr Thr Arg Phe Ser Leu Ala Arg Gln Val Asp Gly Asp
20 25 30

Asn Ser His Val Glu Met Lys Leu Ala Val Asp Glu Glu Glu Asn Ala
35 40 45

Asp Asn Asn Thr Lys Ala Asn Val Thr Lys Pro Lys Arg Cys Ser Gly
50 55 60

Ser Ile Cys Tyr Gly Thr Ile Ala Val Ile Val Phe Phe Leu Ile Gly
65 70 75 80

Phe Met Ile Gly Tyr Leu Gly Tyr Cys Lys Gly Val Glu Pro Lys Thr
85 90 95

Glu Cys Glu Arg Leu Ala Gly Thr Glu Ser Pro Val Arg Glu Glu Pro
100 105 110

Gly Glu Asp Phe Pro Ala Ala Arg Arg Leu Tyr Trp Asp Asp Leu Lys
115 120 125

Arg Lys Leu Ser Glu Lys Leu Asp Ser Thr Asp Phe Thr Gly Thr Ile
130 135 140

Lys Leu Leu Asn Glu Asn Ser Tyr Val Pro Arg Glu Ala Gly Ser Gln
145 150 155 160

Lys Asp Glu Asn Leu Ala Leu Tyr Val Glu Asn Gln Phe Arg Glu Phe
165 170 175

Lys Leu Ser Lys Val Trp Arg Asp Gln His Phe Val Lys Ile Gln Val
180 185 190

Lys Asp Ser Ala Gln Asn Ser Val Ile Ile Val Asp Lys Asn Gly Arg
195 200 205

Leu Val Tyr Leu Val Glu Asn Pro Gly Gly Tyr Val Ala Tyr Ser Lys
210 215 220

Ala Ala Thr Val Thr Gly Lys Leu Val His Ala Asn Phe Gly Thr Lys
225 230 235 240

Lys Asp Phe Glu Asp Leu Tyr Thr Pro Val Asn Gly Ser Ile Val Ile
245 250 255

Val Arg Ala Gly Lys Ile Thr Phe Ala Glu Lys Val Ala Asn Ala Glu
260 265 270

Ser Leu Asn Ala Ile Gly Val Leu Ile Tyr Met Asp Gln Thr Lys Phe
275 280 285

Pro Ile Val Asn Ala Glu Leu Ser Phe Phe Gly His Ala His Leu Gly
290 295 300

Thr Gly Asp Pro Tyr Thr Pro Gly Phe Pro Ser Phe Asn His Thr Gln

305		310		315		320									
Phe	Pro	Pro	Ser	Arg	Ser	Ser	Gly	Leu	Pro	Asn	Ile	Pro	Val	Gln	Thr
				325					330					335	
Ile	Ser	Arg	Ala	Ala	Ala	Glu	Lys	Leu	Phe	Gly	Asn	Met	Glu	Gly	Asp
			340					345					350		
Cys	Pro	Ser	Asp	Trp	Lys	Thr	Asp	Ser	Thr	Cys	Arg	Met	Val	Thr	Ser
		355					360					365			
Glu	Ser	Lys	Asn	Val	Lys	Leu	Thr	Val	Ser	Asn	Val	Leu	Lys	Glu	Ile
	370					375					380				
Lys	Ile	Leu	Asn	Ile	Phe	Gly	Val	Ile	Lys	Gly	Phe	Val	Glu	Pro	Asp
385					390					395					400
His	Tyr	Val	Val	Val	Gly	Ala	Gln	Arg	Asp	Ala	Trp	Gly	Pro	Gly	Ala
				405					410					415	
Ala	Lys	Ser	Gly	Val	Gly	Thr	Ala	Leu	Leu	Leu	Lys	Leu	Ala	Gln	Met
			420					425					430		
Phe	Ser	Asp	Met	Val	Leu	Lys	Asp	Gly	Phe	Gln	Pro	Ser	Arg	Ser	Ile
		435					440					445			
Ile	Phe	Ala	Ser	Trp	Ser	Ala	Gly	Asp	Phe	Gly	Ser	Val	Gly	Ala	Thr
	450					455					460				
Glu	Trp	Leu	Glu	Gly	Tyr	Leu	Ser	Ser	Leu	His	Leu	Lys	Ala	Phe	Thr
465					470					475					480
Tyr	Ile	Asn	Leu	Asp	Lys	Ala	Val	Leu	Gly	Thr	Ser	Asn	Phe	Lys	Val
				485					490					495	
Ser	Ala	Ser	Pro	Leu	Leu	Tyr	Thr	Leu	Ile	Glu	Lys	Thr	Met	Gln	Asn
			500					505					510		

Val Lys His Pro Val Thr Gly Gln Phe Leu Tyr Gln Asp Ser Asn Trp
515 520 525

Ala Ser Lys Val Glu Lys Leu Thr Leu Asp Asn Ala Ala Phe Pro Phe
530 535 540

Leu Ala Tyr Ser Gly Ile Pro Ala Val Ser Phe Cys Phe Cys Glu Asp
545 550 555 560

Thr Asp Tyr Pro Tyr Leu Gly Thr Thr Met Asp Thr Tyr Lys Glu Leu
565 570 575

Ile Glu Arg Ile Pro Glu Leu Asn Lys Val Ala Arg Ala Ala Glu
580 585 590

Val Ala Gly Gln Phe Val Ile Lys Leu Thr His Asp Val Glu Leu Asn
595 600 605

Leu Asp Tyr Glu Arg Tyr Asn Ser Gln Leu Leu Ser Phe Val Arg Asp
610 615 620

Leu Asn Gln Tyr Arg Ala Asp Ile Lys Glu Met Gly Leu Ser Leu Gln
625 630 635 640

Trp Leu Tyr Ser Ala Arg Gly Asp Phe Phe Arg Ala Thr Ser Arg Leu
645 650 655

Thr Thr Asp Phe Gly Asn Ala Glu Lys Thr Asp Arg Phe Val Met Lys
660 665 670

Lys Leu Asn Asp Arg Val Met Arg Val Glu Tyr His Phe Leu Ser Pro
675 680 685

Tyr Val Ser Pro Lys Glu Ser Pro Phe Arg His Val Phe Trp Gly Ser
690 695 700

Gly Ser His Thr Leu Pro Ala Leu Leu Glu Asn Leu Lys Leu Arg Lys
705 710 715 720

Gln Asn Asn Gly Ala Phe Asn Glu Thr Leu Phe Arg Asn Gln Leu Ala
725 730 735

Leu Ala Thr Trp Thr Ile Gln Gly Ala Ala Asn Ala Leu Ser Gly Asp
740 745 750

Val Trp Asp Ile Asp Asn Glu Phe
755 760

<210> 58
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of an exemplified linker 1

<400> 58

Gly Gly Gly Gly Ser
1 5

<210> 59
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of an exemplified linker 2

<400> 59

Gly Gly Gly Gly Gly Ser
1 5

<210> 60
<211> 5
<212> PRT
<213> Artificial Sequence

<220>

<223> amino acid sequence of an exemplified linker 3

<400> 60

Ser Gly Gly Gly Gly
1 5

<210> 61

<211> 219

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of the light-chain of anti-hTfR antibody

<400> 61

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ser Gln Ser
85 90 95

Thr His Val Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu

115

120

125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 145 150 155 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 210 215

<210> 62

<211> 448

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of the heavy-chain of anti-hTfR antibody

<400> 62

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
 1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Asn Tyr
 20 25 30

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
 35 40 45

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
50 55 60

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225 230 235 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg

245

250

255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
 260 265 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
 275 280 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
 290 295 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
 305 310 315 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
 325 330 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
 340 345 350

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
 355 360 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
 370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
 385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
 405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
 420 425 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
 435 440 445

<210> 63
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<223> amino acid sequence of Fab heavy chain of anti-hTfR antibody

<400> 63

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Met Asn Tyr
20 25 30

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
50 55 60

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
195 200 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
210 215 220

His Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
225 230 235 240

Ser Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg
245 250 255

Leu Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg
260 265 270

Ala Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly
275 280 285

Gly Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala
290 295 300

Ala Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val
305 310 315 320

Ala Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val
325 330 335

Pro Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln
340 345 350

Asn Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg
355 360 365

Trp Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala
370 375 380

Leu Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala
385 390 395 400

Leu Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala
405 410 415

Phe Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro
420 425 430

Leu Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val
435 440 445

Leu Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe

450

455

460

Ala Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn
 465 470 475 480

Val Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys
 485 490 495

Ser Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser
 500 505 510

Leu Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr
 515 520 525

Gly Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser
 530 535 540

Tyr Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val
 545 550 555 560

Asp Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln
 565 570 575

Pro Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val
 580 585 590

Pro Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro
 595 600 605

Val Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys
 610 615 620

Met Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu
 625 630 635 640

Ala Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr
 645 650 655

Met Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val
660 665 670

Val Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro
675 680 685

Asp Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val
690 695 700

Ser His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val
705 710 715 720

Tyr Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu
725 730 735

Val Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg
740 745 750

Ser Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser
755 760 765

Leu Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg
770 775 780

Gln Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser
785 790 795 800

Ala Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val
805 810 815

Leu Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp
820 825 830

Ser Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala
835 840 845

Val Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln
850 855 860

Leu Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys
865 870 875 880

Gln Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu
885 890 895

Phe Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln
900 905 910

Gln His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val
915 920 925

Leu Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp
930 935 940

Leu Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly
945 950 955 960

Ser Trp

<210> 65

<211> 962

<212> PRT

<213> Artificial Sequence

<220>

<223> amino acid sequence of fusion protein of hNAGLU mutant type 9 and
Fab heavy chain of anti-hTfR antibody (2)

<400> 65

Asp Glu Ala Arg Glu Ala Ala Ala Val Arg Ala Leu Val Ala Arg Leu
1 5 10 15

Leu Gly Pro Gly Pro Ala Ala Asp Phe Ser Val Ser Val Glu Arg Ala

20

25

30

Leu Ala Ala Lys Pro Gly Leu Asp Thr Tyr Ser Leu Ser Gly Gly Gly
 35 40 45

Gly Ala Ala Arg Val Arg Val Arg Gly Ser Thr Gly Val Ala Ala Ala
 50 55 60

Ala Gly Leu His Arg Tyr Leu Arg Asp Phe Cys Gly Cys His Val Ala
 65 70 75 80

Trp Ser Gly Ser Gln Leu Arg Leu Pro Arg Pro Leu Pro Ala Val Pro
 85 90 95

Gly Glu Leu Thr Glu Ala Thr Pro Asn Arg Tyr Arg Tyr Tyr Gln Asn
 100 105 110

Val Cys Thr Gln Ser Tyr Ser Phe Val Trp Trp Asp Trp Ala Arg Trp
 115 120 125

Glu Arg Glu Ile Asp Trp Met Ala Leu Asn Gly Ile Asn Leu Ala Leu
 130 135 140

Ala Trp Ser Gly Gln Glu Ala Ile Trp Gln Arg Val Tyr Leu Ala Leu
 145 150 155 160

Gly Leu Thr Gln Ala Glu Ile Asn Glu Phe Phe Thr Gly Pro Ala Phe
 165 170 175

Leu Ala Trp Gly Arg Met Gly Asn Leu His Thr Trp Asp Gly Pro Leu
 180 185 190

Pro Pro Ser Trp His Ile Lys Gln Leu Tyr Leu Gln His Arg Val Leu
 195 200 205

Asp Arg Met Arg Ser Phe Gly Met Thr Pro Val Leu Pro Ala Phe Ala
 210 215 220

Gly His Val Pro Glu Ala Val Thr Arg Val Phe Pro Gln Val Asn Val
225 230 235 240

Thr Lys Met Gly Ser Trp Gly His Phe Asn Cys Ser Tyr Ser Cys Ser
245 250 255

Phe Leu Leu Ala Pro Glu Asp Pro Ile Phe Pro Ile Ile Gly Ser Leu
260 265 270

Phe Leu Arg Glu Leu Ile Lys Glu Phe Gly Thr Asp His Ile Tyr Gly
275 280 285

Ala Asp Thr Phe Asn Glu Met Gln Pro Pro Ser Ser Glu Pro Ser Tyr
290 295 300

Leu Ala Ala Ala Thr Thr Ala Val Tyr Glu Ala Met Thr Ala Val Asp
305 310 315 320

Thr Glu Ala Val Trp Leu Leu Gln Gly Trp Leu Phe Gln His Gln Pro
325 330 335

Gln Phe Trp Gly Pro Ala Gln Ile Arg Ala Val Leu Gly Ala Val Pro
340 345 350

Arg Gly Arg Leu Leu Val Leu Asp Leu Phe Ala Glu Ser Gln Pro Val
355 360 365

Tyr Thr Arg Thr Ala Ser Phe Gln Gly Gln Pro Phe Ile Trp Cys Met
370 375 380

Leu His Asn Phe Gly Gly Asn His Gly Leu Phe Gly Ala Leu Glu Ala
385 390 395 400

Val Asn Gly Gly Pro Glu Ala Ala Arg Leu Phe Pro Asn Ser Thr Met
405 410 415

Val Gly Thr Gly Met Ala Pro Glu Gly Ile Ser Gln Asn Glu Val Val
420 425 430

Tyr Ser Leu Met Ala Glu Leu Gly Trp Arg Lys Asp Pro Val Pro Asp
435 440 445

Leu Ala Ala Trp Val Thr Ser Phe Ala Ala Arg Arg Tyr Gly Val Ser
450 455 460

His Pro Asp Ala Gly Ala Ala Trp Arg Leu Leu Leu Arg Ser Val Tyr
465 470 475 480

Asn Cys Ser Gly Glu Ala Cys Arg Gly His Asn Arg Ser Pro Leu Val
485 490 495

Arg Arg Pro Ser Leu Gln Met Asn Thr Ser Ile Trp Tyr Asn Arg Ser
500 505 510

Asp Val Phe Glu Ala Trp Arg Leu Leu Leu Thr Ser Ala Pro Ser Leu
515 520 525

Ala Thr Ser Pro Ala Phe Arg Tyr Asp Leu Leu Asp Leu Thr Arg Gln
530 535 540

Ala Val Gln Glu Leu Val Ser Leu Tyr Tyr Glu Glu Ala Arg Ser Ala
545 550 555 560

Tyr Leu Ser Lys Glu Leu Ala Ser Leu Leu Arg Ala Gly Gly Val Leu
565 570 575

Ala Tyr Glu Leu Leu Pro Ala Leu Asp Glu Val Leu Ala Ser Asp Ser
580 585 590

Arg Phe Leu Leu Gly Ser Trp Leu Glu Gln Ala Arg Ala Ala Ala Val
595 600 605

Ser Glu Ala Glu Ala Asp Phe Tyr Glu Gln Asn Ser Arg Tyr Gln Leu
610 615 620

Thr Leu Trp Gly Pro Glu Gly Asn Ile Leu Asp Tyr Ala Asn Lys Gln
625 630 635 640

Leu Ala Gly Leu Val Ala Asn Tyr Tyr Thr Pro Arg Trp Arg Leu Phe
645 650 655

Leu Glu Ala Leu Val Asp Ser Val Ala Gln Gly Ile Pro Phe Gln Gln
660 665 670

His Gln Phe Asp Lys Asn Val Phe Gln Leu Glu Gln Ala Phe Val Leu
675 680 685

Ser Lys Gln Arg Tyr Pro Ser Gln Pro Arg Gly Asp Thr Val Asp Leu
690 695 700

Ala Lys Lys Ile Phe Leu Lys Tyr Tyr Pro Arg Trp Val Ala Gly Ser
705 710 715 720

Trp Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
725 730 735

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
740 745 750

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Met Asn Tyr
755 760 765

Trp Leu Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
770 775 780

Gly Asp Ile Tyr Pro Gly Gly Asp Tyr Pro Thr Tyr Ser Glu Lys Phe
785 790 795 800

Lys Val Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr

805

810

815

Leu Gln Leu Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
 820 825 830

Ala Arg Ser Gly Asn Tyr Asp Glu Val Ala Tyr Trp Gly Gln Gly Thr
 835 840 845

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
 850 855 860

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
 865 870 875 880

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
 885 890 895

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
 900 905 910

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
 915 920 925

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
 930 935 940

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr
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His Thr

<210> 66

<211> 740

<212> DNA

<213> Artificial Sequence

<220>

<223> nucleotide sequence encoding the amino acid sequence of the light chain of anti-hTfR antibody, synthetic sequence

<400> 66

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cagcctgcca gcatcagctg cagaagctct cagagcctgg tgcacagcaa cggcaacacc      180
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gctcccagcg tgttcatctt cccacctagc gacgagcagc tgaagtccgg cacagcctct      480
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acctacagcc tgagcagcac cctgaccctg agcaaggccg actacgagaa gcacaagggtg      660
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ggcgagtgtc aagcggccgc                                     740
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<210> 67

<211> 23

<212> PRT

<213> Homo sapiens

<400> 67

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Gly Ala Gly Gly Ala Ala Gly
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